Targeted Gene Correction of Laminopathy-Associated LMNA Mutations in Patient-Specific iPSCs.

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Public Summary:
Combination of stem cell-based approaches with gene-editing technologies represents an attractive strategy for studying human disease and developing therapies. However, gene-editing methodologies described to date for human cells suffer from technical limitations including limited target gene size, low targeting efficiency at transcriptionally inactive loci, and off-target genetic effects that could hamper broad clinical application. To address these limitations, and as a proof of principle, we focused on homologous recombination-based gene correction of multiple mutations on lamin A (LMNA), which are associated with various degenerative diseases. We show that helper-dependent adenoviral vectors (HDAdVs) provide a highly efficient and safe method for correcting mutations in large genomic regions in human induced pluripotent stem cells and can also be effective in adult human mesenchymal stem cells. This type of approach could be used to generate genotype-matched cell lines for disease modeling and drug discovery and potentially also in therapeutics

Scientific Abstract:
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